LISTING OF THE CLAIMS

This listing of claims will replace all prior versions and listings of claims in the application:

1. (Previously Presented) A method of diagnosis of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jakob Disease (CJD) or the possibility thereof in a subject suspected of suffering from BSE or CJD, which comprises subjecting a sample of a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE- or CJD- infected subjects and non- BSE- or CJD- infected subjects, and is selected from the group consisting of (a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da;
(b) cystatin C; and
(c) a hemoglobin, a hemoglobin chain, or a truncated chain or fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin;
comparing the test amount of the polypeptide in the sample to a reference amount of the polypeptide, wherein the reference amount of the polypeptide represents no BSE or CJD infection; and wherein an increase or decrease in the polypeptide in the subject's body fluid compared to the reference indicates BSE or CJD in the subject.

2. (Previously Presented) The method according to Claim 1, in which the polypeptide is present in the body fluid of BSE- or CJD- infected subjects and not present in the body fluid of non- BSE- or CJD-infected subjects, whereby the presence of the polypeptide in a body fluid sample is indicative of BSE or CJD .

3. (Previously Presented) The method according to Claim 1, in which the polypeptide is not present in the body fluid of BSE- or CJD- infected subjects and present in the body fluid of non- BSE- or CJD-infected subjects, whereby the non-presence of the polypeptide in a body fluid sample is indicative of BSE or CJD.

4. (Previously Presented) The method according to Claim 1, in which the mass spectrometry is laser desorption/ionization mass spectrometry.

5. (Previously Amended) The method according to Claim 4, in which the sample is adsorbed on a probe or on a protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic or weak cationic exchange surface capable of binding the polypeptide.

6. (Previously Presented) The method according to Claim 4, in which the polypeptide is determined by surface-enhanced laser desorption/ionization (SELDI) and time of flight mass spectrometry (TOF-MS).

7. (Canceled).

8. (Previously Presented) The method according to Claim 1, in which a plurality of peptides is determined in the sample.

9. (Previously Presented) The method according to Claim 1, in which the TSE is Creutzfeldt-Jakob disease (CJD).

10. (Previously Presented) The method according to Claim 9, in which the TSE is sporadic Creutzfeldt-Jakob Disease (CJD) or variant Creutzfeldt-Jakob Disease (CJD).

11. (Previously Presented) The method according to Claim 9, in which one or more polypeptides having a respective molecular weight of about 4780, about 6700, about 8600 or

about 13375 Da is determined, and the presence of one or more of such polypeptides is indicative of CJD.

12. (Previously Presented) The method according to Claim 9 in which one or more polypeptides having a respective molecular weight of about 3970, about 3990, about 4294, about 4478, about 10075, about 11730, about 14043 or about 17839 Da is determined, and the absence of one or more of such polypeptides is indicative of CJD.

13. (Previously Presented) The method according to Claim 9, in which a polypeptide having a molecular weight of about 7770 Da is determined, and the presence of such polypeptide is indicative of CJD.

14. (Previously Presented) The method according to Claim 9, in which a polypeptide having a molecular weight of about 3295, about 4315, about 4436, about 6200, about 8936, about 9107, about 9145, about 9185, about 9454 or about 13550 Da is determined, and the absence or decreased amount of one or more of such polypeptides is indicative of CJD.

15. (Previously Presented) The method according to Claim 9, in which a polypeptide having a molecular weight of about 7574, about 7930, about 7975 or about 8020 Da is determined, and the presence or increased amount of one or more of such polypeptides is indicative of CJD.

16. (Previously Presented) The method according to Claim 1, in which the TSE is Bovine Spongiform Encephalopathy (BSE).

17. (Previously Presented) The method according to Claim 16, in which the polypeptide has a molecular weight of about 10220 Da, and the presence of the polypeptide is indicative of BSE.

18. (Previously Presented) The method according to Claim 16, in which one or more polypeptides having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030,

3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da is determined, and the differential expression of one or more of such polypeptides is indicative of BSE.

19. (Previously Presented) The method according to Claim 1, in which the TSE is scrapie.

20. (Withdrawn) A method of diagnosis, prognosis or therapy which comprises use of a polypeptide which is differentially contained in a body fluid of TSE-infected subjects and non-infected subjects, the polypeptide having a molecular weight in the range of from 1000 to 100000 and being determinable by mass spectrometry.

21. (Previously Presented) A method of diagnosis, prognosis or therapy of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jakob Disease (CJD) comprising contacting a material which recognizes, binds to or has affinity for a polypeptide which is differentially contained in a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum of BSE- or CJD- infected subjects and non-infected subjects, the polypeptide being selected from the group consisting of

(a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da;

(b) cystatin C; and

(c) a hemoglobin, a hemoglobin chain, or a truncated chain or fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin;

and being determinable by mass spectrometry, wherein the amount of polypeptide in a sample is compared to a reference amount of polypeptide wherein the reference amount of polypeptide represents no BSE- or CJD- infection.

22. (Previously Presented) The method according to Claim 21, in which the material is an antibody or antibody chip.

23. (Withdrawn) An assay device for use in the diagnosis of TSE which comprises a plate having a location containing a material which recognizes, binds to or has affinity for a polypeptide which is differentially contained in a body fluid of TSE-infected subjects and non-infected subjects, the polypeptide having a molecular weight in the range of from 1000 to 100000 and being determinable by mass spectrometry.

24. (Withdrawn) An assay device for use in the diagnosis of TSE, which comprises a plate having a location containing an antibody that is specific for cystatin C.

25. (Withdrawn) An assay device for use in the diagnosis of variant CJD, which comprises a plate having a location containing an antibody that is specific for cystatin C and useful in the diagnosis of variant CJD.

26. (Withdrawn) An assay device for use in the diagnosis of sporadic CJD, which comprises a plate having a location containing an antibody that is specific for cystatin C and useful in the diagnosis of sporadic CJD.

27. (Withdrawn) An assay device for use in the diagnosis of BSE, which comprises a plate having a location containing an antibody that is specific for a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof having an immunological reaction to antibodies specific for bovine hemoglobin and useful in the diagnosis of BSE.

28. (Withdrawn) An assay device for use in the diagnosis of a TSE comprising a solid substrate having attached thereto an antibody that is specific for any of the following:

(i) a polypeptide that is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and has a molecular weight in the range of from 1000 to 100000;

(ii) a polypeptide that is differentially contained in the body fluid of TSE-infected subjects and non-TSE-infected subjects, and is selected from those having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da

(iii) cystatin C;

(iv) a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin and is differentially contained in the body tissue of bovine TSE-infected subjects and non-bovine non-TSE-infected subjects.

29. (Previously Presented) A kit for diagnosis of a TSE selected from the group consisting of BSE and CJD, comprising a probe or protein chip array having an immobilized metal affinity capture (IMAC), hydrophobic, strong anionic, or weak cationic exchange surface capable of binding a polypeptide onto which a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma, and serum is adsorbed, and for placement in a mass spectrometer, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE- or CJD- infected subjects and non- BSE- or CJD- infected subjects, and is selected from the group consisting of (a) a polypeptide having a molecular weight of about 1010, 1100, 1125, 1365, 3295, 3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da;

(b) cystatin C; and

(c) a hemoglobin, a hemoglobin chain, or a truncated chain or fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin;

wherein diagnosis of TSE is determined by comparing the test amount of polypeptide to a reference amount of polypeptide, wherein the reference amount of polypeptide represents no BSE or CJD infection.

30. (Previously Presented) The kit according to Claim 29, in which the probe contains an adsorbent for adsorption of the polypeptide.

31. (Previously Presented) The kit according to Claim 29, further comprising a washing solution for removal of unbound or weakly bound materials from the probe.

32. (Previously Presented) A method of diagnosis of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jakob Disease (CJD) or the possibility thereof in a subject suspected of suffering from BSE or CJD, which comprises determining a test amount of cystatin C in a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject, wherein the cystatin C is differentially contained in the body fluid of BSE- or CJD- infected subjects and non-TSE-infected subjects; comparing the test amount of cystatin C in the sample to a reference amount of cystatin C wherein the reference amount of cystatin C represents no BSE or CJD infection; and wherein an increase of cystatin C in the body fluid of the subject indicates BSE or CJD.

33. (Previously Presented) A method of diagnosis of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of BSE Bovine Spongiform Encephalopathy and Creutzfeldt-Jakob Disease (CJD) or the possibility thereof in a subject suspected of suffering from the BSE or CJD, which comprises subjecting a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject to mass spectrometry, thereby to determine a test amount of cystatin C in the sample, wherein the cystatin C is differentially contained in the body fluid of BSE- or CJD-infected subjects and non-BSE- or CJD- infected subjects, comparing the test amount of cystatin C in the sample to a reference amount of cystatin C, wherein the reference amount of polypeptide represents no BSE or CJD infection; and wherein an increase in cystatin C in the body fluid of the subject indicates BSE or CJD.

34. (Previously Presented) The method of claim 33, wherein the body fluid is cerebrospinal fluid (CSF).

35. (Previously Presented) A method of diagnosis of Bovine Spongiform Encephalopathy (BSE) or the possibility thereof in a bovine subject suspected of suffering from BSE, which comprises determining a test amount of a polypeptide in a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject, wherein the polypeptide is differentially contained in the body fluid of BSE infected bovine subjects and non- BSE- infected subjects, and wherein the polypeptide is selected from the group consisting of a hemoglobin, a hemoglobin chain a truncated chain and a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin; comparing the test amount of the polypeptide in the sample to a reference amount of the polypeptide, wherein the reference amount of polypeptide represents no BSE infection; and wherein an increase in the polypeptide in the body fluid of the subject indicates BSE.

36. (Previously Presented) A method of diagnosis of Bovine Spongiform Encephalopathy (BSE) or the possibility thereof in a bovine subject suspected of suffering from the BSE, which comprises subjecting a sample of body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum taken from the subject to mass spectrometry, thereby to determine a test amount of a polypeptide in the sample, wherein the polypeptide is differentially contained in the body fluid of BSE- infected bovine subjects and non- BSE- infected subjects, wherein the polypeptide is a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin; comparing the test amount of the polypeptide in the sample to a reference amount of the polypeptide, wherein the reference amount of polypeptide represents no BSE infection; and wherein an increase in the polypeptide in the body fluid of the subject indicates diagnosis of BSE.

37. (Previously Presented) A method of providing an indication of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jakob Disease (CJD) or the possibility or progress thereof in a subject liable to suffer from BSE or CJD, which comprises use as a marker of a level of at least one polypeptide that has a molecular weight, of about 1010, 1100, 1125, 1365, 3295,

3645, 3890, 3970, 3990, 4030, 4294, 4315, 4436, 4478, 4780, 5820, 6200, 6700, 7520, 7574, 7630, 7770, 7930, 7975, 7980, 8020, 8600, 8936, 9107, 9145, 9185, 9454, 9950, 10075, 10220, 10250, 11600, 11730, 11800, 13375, 13550, 14043, 15000, 15200, 15400, 15600, 15900, 17839, 30000, 31000 or 31800 Da that is measurable or detectable by mass spectrometry and is differentially contained in a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum of BSE- or CJD- infected subjects and non- BSE- or CJD- infected subjects wherein the amount of polypeptide in a sample is compared to a reference amount of polypeptide, wherein the reference amount of polypeptide represents no BSE or CJD infection.

38. (Original) The method of claim 37, wherein said at least one polypeptide is selected from those having a respective molecular weight of about 1010, 1100, 1125, 1365, 3645, 4030, 3890, 5820, 7520, 7630, 7980, 9950, 10250, 11600, 11800, 15000, 15200, 15400, 15600, 15900, 30000, 31000 and 31800 Da.

39. (Canceled).

40. (Previously Presented) A method of providing an indication of a transmissible spongiform encephalopathy (TSE) selected from the group consisting of Bovine Spongiform Encephalopathy (BSE) and Creutzfeldt-Jakob Disease (CJD) or the possibility or progress thereof in a subject liable to suffer from BSE or CJD, which comprises use as a marker of a level of cystatin C measurable or detectable by mass spectroscopy and is differentially contained in a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum of BSE- or CJD- infected subjects and non- BSE- or CJD- infected subjects wherein the amount of cystatin C in the sample is compared to a reference amount of cystatin C, wherein the reference amount of cystatin C represents no BSE or CJD infection.

41. (Previously Presented) The method of claim 40, wherein the TSE is CJD and the body fluid is from a human subject.

42. (Previously Presented) The method of claim 40, wherein the body fluid is cerebrospinal fluid (CSF).

43. (Previously Presented) A method of providing an indication of Bovine Spongiform Encephalopathy (BSE) or the possibility or progress thereof in a bovine subject liable to suffer from BSE, which comprises use as a marker of a level of a hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof which exhibits an immunological reaction to an antibody to bovine hemoglobin, said level being measurable or detectable by mass spectroscopy, and said hemoglobin, hemoglobin chain or truncated chain or fragment thereof being differentially contained in a body fluid selected from the group consisting of cerebrospinal fluid (CSF), blood, plasma and serum of bovine BSE- infected subjects and non-bovine non-BSE- infected subjects, wherein the amount of hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof in the sample is compared to a reference amount of hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof, wherein the reference amount of hemoglobin, a hemoglobin chain or a truncated chain or a fragment thereof represents no BSE infection.

44. (Original) The method of claim 43, wherein said hemoglobin, hemoglobin chain or truncated chain or fragment thereof has a molecular weight determinable by mass spectroscopy of about 15000 Da, 7500 Da or 3000 Da.

45. (Previously Presented) The method of claim 43, wherein the sample of body fluid is plasma.

46. (Previously Presented) The method of claim 43, wherein the sample of body fluid is from a living animal.

47. (Withdrawn) A bovine animal, or herd of said animals, that has or have been subjected to a test as defined in claim 43 and found to be free of a transmissible spongiform encephalopathy (TSE).